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10/595,948	05/22/2006	Tomoki Kato	PC26223A	9541

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EXAMINER	
GOON, SCARLETT Y	
ART UNIT	PAPER NUMBER
1623	

NOTIFICATION DATE	DELIVERY MODE
07/21/2009	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/595,948	KATO ET AL.	
	Examiner	Art Unit	
	SCARLETT GOON	1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 April 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *15-28* is/are pending in the application.

4a) Of the above claim(s) *26-28* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *15-21,24 and 25* is/are rejected.

7)☒ Claim(s) *22 and 23* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *31 August 2006*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The preliminary amendment filed on 22 May 2006 in which claims 1-14 were cancelled, and claims 15-28 were newly added, is again acknowledged.

Claims 15-28 are pending in the instant application.

Priority

This application is a National Stage entry of PCT/IB2004/003707 filed on 10 November 2004 and claims priority to U.S. provisional application no 60/524,681 filed on 24 November 2003.

Information Disclosure Statement

The information disclosure statement (IDS) dated 31 August 2006 complies with the provisions of 37 CFR 1.97, 1.98 and MPEP § 609. Accordingly, it has been placed in the application file and the information therein has been considered as to the merits.

Election/Restrictions

Applicant's election without traverse of Group I, claims 15-25, drawn to a compound of formula (I) in the reply filed on 17 April 2009 is acknowledged. In response to a requirement for an election of species, Applicants further elected *N*-({1-[(*trans*-1,4-dihydroxycyclohexyl)methyl]piperidin-4-yl}methyl)-1-isopropyl-5-methyl-2-oxo-1,2-dihydroquinoline-3-carboxamide ethanedioate, as disclosed in Example 10 of the instant Specification.

The requirement is still deemed proper and is therefore made FINAL.

Claims 26-28 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 17 April 2009.

Claims 15-25 will be examined on its merits herein.

Applicants' elected species and the remaining species of claim 23, the cis isomer of the elected species, is not fairly suggested in the prior art. Thus, the search has been extended to include the full scope of claim 22 and generic claim 15.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Section [0001]

Claims 15-21, 24 and 25 are rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 6,951,867 B2 to Katsu *et al.* (herein referred to as the '867 patent; PTO-892, Ref. A) in view of Suzuki *et al.* (of record).

The Katsu '867 patent teaches compounds of formula (I) having 5-HT4 receptor binding activity, and thus are useful in a pharmaceutical composition for the treatment of gastroesophageal reflux disease, non-ulcer dyspepsia, functional dyspepsia, irritable bowel syndrome or the like (column 1, lines 13-24). Other than the difference of a imidazopyridine ring, the compounds of formula (I) are similar to that of the instantly claimed invention when R^3 represents an alkyl group having from 1 to 10 carbon atoms, said alkyl group substituted by at least one substituent selected from the group consisting of aryl groups, hydroxyl groups, oxo groups, aminocarbonyl groups, mono- or di-alkylaminocarbonyl groups having from 1 to 6 carbon atoms, alkylsulfonylamino

groups having from 1 to 6 carbon atoms, heterocyclic groups, heterocycliccarbonyl groups and a cycloalkyl group having from 3 to 8 carbon atoms (column 3, lines 1-23). Heterocyclic compounds means those having a 5- to 10-membered monocyclic or bicyclic ring which may be saturated, partially saturated, or aromatic, and which consists of carbon atoms and from 1 to 4 heteroatoms independently selected from the group consisting of N, O, and S (column 4, line 66 – column 5, line 4). Preferred heterocyclic compounds include piperidino, morpholino, piperidinyl, morpholinyl, quinolyl, among others (column 5, lines 27-33). The imidazopyridine compounds can be administered via either the oral, parenteral or topical routes to mammals (column 26, lines 45-47). In general, the compounds are most desirably administered to humans in dose ranges ranging from about 0.3 mg to about 750 mg per day, preferably from about 10 mg to about 500 mg per day, although variations will necessarily occur depending upon the weight and condition of the subject being treated, the disease state being treated, and the particular route of administration chosen (column 26, lines 47-54). The compounds may be administered alone or in combination with pharmaceutically acceptable carriers or diluents (column 26, lines 57-59).

The difference between the teachings of the Katsu '867 patent and that of the instantly claimed invention is the presence of an imidazopyridine structure where the instant claims have a quinoline carboxylic acid structure.

Suzuki *et al.* teach the synthesis and evaluation of quinolinecarboxamide derivatives as serotonin 5-HT4 receptor agonists. Known classes of compounds for stimulating 5-HT4 receptors include the indolealkylamines, the benzamides, and the

benzimidazolones (p. 2003, column 1, paragraph 2). Suzuki *et al.* teach that while there are numerous reports on the modification of the group connected to the amide bond of these compounds, there are relatively few reports concerning modifications of the aromatic ring moiety of these same compounds (p. 2003, column 1, paragraph 2). Towards this end, Suzuki *et al.* studied quinolinecarboxamide derivatives as 5-HT4 receptor agonists and showed that these compounds, particularly 8c (Figure 4), exhibited high and specific 5-HT4 receptor-stimulating activity. Thus, these represent promising compounds for the improvement of gastrointestinal dysfunction (p. 2005-2006, bridging sentence).

With regards to the substitution of a methyl group in place of a hydrogen on the aryl ring of the quinolinecarboxamide derivative, one of ordinary skill in the art would have found the modification *prima facie* obvious because it is well established that the substitution of a methyl for hydrogen on a known compound is not a patentable modification absent unexpected or unobvious results. See *In re Lincoln*, 126 USPQ 477, 53 USPQ 40 (CCPA 1942); *In re Druey*, 319 F.2d 237, 138 USPQ 39 (CCPA 1963); *In re Lohr*, 317 F.2d 388, 137 USPQ 548 (CCPA 1963); *In re Hoehsema*, 399 F.2d 269, 158 USPQ 598 (CCPA 1968); *In re Wood*, 582 F.2d 638, 199 USPQ 137 (CCPA 1978); *In re Hoke*, 560 F.2d 436, 195 USPQ 148 (CCPA 1977); *Ex parte Fauque*, 121 USPQ 425 (POBA 1954); *Ex parte Henkel*, 130 USPQ 474 (POBA 1960).

It would have been obvious to one of ordinary skill in the art at the time of the invention to combine the teachings of the Katsu '867 patent, concerning compounds of formula (I) having 5-HT4 receptor binding activity, with the teachings of Suzuki *et al.*,

regarding quinolinecarboxamide derivatives as serotonin 5-HT4 receptor agonists. One would have been motivated to combine the teachings in order to receive the expected benefit, as suggested by Suzuki *et al.*, that quinolinecarboxamides represent another modification to the aromatic moiety of compounds that can stimulate 5-HT4 receptors. One of ordinary skill in the art would have been further motivated to make such a substitution based on the teachings of Suzuki *et al.* that the quinolinecarboxamides exhibit high and specific 5-HT4 receptor stimulating activity and is a promising compound for the improvement of gastrointestinal dysfunction.

Thus, the claimed invention as a whole is *prima facie* obvious over the combined teachings of the prior art.

Section [0002]

Claims 15-20, 24 and 25 are rejected under 35 U.S.C. 103(a) as being unpatentable over JP 09-194374 to Ouchi *et al.* (IDS dated 31 August 2006, machine translation) in view of EP 0382687 to Micheletti *et al.* (PTO-892, Ref. N).

Ouchi *et al.* teach therapeutic agents for diseases in the digestive organ, comprising a specific quinoline derivative as an active agent which has excellent stimulating actions on serotonin 4 receptors (abstract). These compositions are useful for improving chronic gastritis, postoperative gastric motion, pyrosis, anorexia, regurgitant esophagitis, etc. (abstract). One such therapeutic agent is indicated as formula (II) (PAJ, page 3, column 1). The dose of the active agent changes with symptom, but is in the range of 0.01-50 mg for intravenous administration and 0.001-

10mg for internal use (paragraph 0067). It can be prepared for use as solid preparations, such as a tablet, a pill, a capsule, etc (paragraph 0068). Furthermore, it can be manufactured using the usual additives, excipients, disintegrator, binder, lubricant, etc. (paragraph 0069)

The difference between the teachings of Ouchi *et al.* and that of the instantly claimed invention is the presence of an alkylene unit between the amide nitrogen atom and the nitrogen-containing heterocyclic moiety in the instantly claimed structures.

Micheletti *et al.* teach compounds of general formula (I). The compounds are useful for the treatment of gastrointestinal and respiratory tract disorders, including gastrointestinal motility, inhibition of acid secretion, bronchodilation, dry mouth, mydriasis, urinary retention, decreased sweating and tachycardia (p. 3, lines 1-7). Micheletti *et al.* further teach that R_1 and R_2 of the phenyl ring on the quinolone structure may be substituted with H or halogen, among others. The R group may be H or C_{1-6} alkyl; D is C-R when the D-B bond is a double bond; A represents CO or CS; X is an oxygen or N-R; Y is represented by structures (a), (b) or (c) (p. 3, line 38 – p. 4, line 45). Structure (c) is similar to the equivalent group found in formula (II) of Ouchi *et al.*, wherein p connecting to the ring is 0, p in the ring is 1, and q is 2 (p. 4, lines 23-45). Micheletti *et al.* additionally teach that R_6 can be an H, C_{1-4} alkyl, or aralkyl.

It would have been obvious to one of ordinary skill in the art at the time of the invention to combine the teachings of Ouchi *et al.*, concerning quinoline derivatives as active agents for stimulating actions on serotonin 4 receptors and thus are useful for improving chronic gastritis and regurgitant esophagitis, with the teachings of Micheletti

et al., regarding compounds of general formula (I) useful for the treatment of gastrointestinal and respiratory tract disorders. Since the compounds taught by Ouchi *et al.* and Micheletti *et al.* are very similar in structure and are also taught to be used for the same purposes, that being the treatment of gastrointestinal disorders, it would have been *prima facie* obvious for one of ordinary skill in the art to insert a methylene unit between the nitrogen of the amide bond and the amine-containing heterocyclic structure taught by Ouchi *et al.* based on the teachings of Micheletti *et al.* which teach that p (methylene group) can be 0 or 1 at this position. Furthermore, based on the teachings of Micheletti *et al.*, it would have been *prima facie* obvious for one of ordinary skill in the art to substitute a methyl group on the aryl ring of the compound taught by Ouchi *et al.*, to arrive at the structures instantly claimed. Since these compounds have a similar structure and are taught to be used for the same purpose, one of ordinary skill in the art would have been motivated to combine the teachings and make the changes with the expectation that the changes would give predictable results of having similar activity against gastrointestinal disorders. Absent a showing of unexpected results, the instantly claimed compounds are obvious over the teachings of the prior art.

As such, the claimed invention as a whole is *prima facie* obvious over the combined teachings of the prior art.

Allowable Subject Matter

Claims 22 and 23 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to SCARLETT GOON whose telephone number is 571-270-5241. The examiner can normally be reached on Mon - Thu 7:00 am - 4 pm and every other Fri 7:00 am - 12 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shaojia Jiang can be reached on 571-272-0627. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Leigh C. Maier/
Primary Examiner
Art Unit 1623

SCARLETT GOON
Examiner
Art Unit 1623